REMARKS

The present response is intended to be fully responsive to all points of rejection raised by the Examiner and is believed to place the application in condition for allowance. Favorable reconsideration and allowance of the application is respectfully requested.

Applicants assert that the present invention is new, non-obvious and useful. Prompt consideration and allowance of the claims is respectfully requested.

Status of Claims

Claims 1-27 are pending in the application. Claims 14-27 were withdrawn. Claims 1-13 have been rejected. Claims 2, 4, and 5 are canceled herein without prejudice. Claims 1, 3, 6, and 9-10 are amended herein. Support for this amendment can be found, at least, in the claims as filed.

OBJECTIONS

A. Objections to the Drawings

In the Office Action, the Examiner objects to Figure 2. Specifically, the Examiner asserts that the reference characters M1 and M2 are not mentioned in the description. In response, Applicants have amended Figure 2 to remove these reference characters. The amended drawings are concurrently filed herewith. Accordingly, Applicants respectfully request withdrawal of this objection.

B. Objections to the Specification

In the Office Action, the Examiner objects to the specification, as containing the trademark terms. Specifically, the Examiner asserts that the trademark terms TO-PRO and ORACLE are noted in the specification and they should be capitalized. In response, Applicants have amended the specification to capitalize the trademark terms, and therefore Applicants respectfully request withdrawal of this objection.

C. Objection to the Claims

In the Office Action, the Examiner objects to claim 1, as containing a spelling error in the term "proliferation." In response, Applicants note that Applicants have amended claim 1. The amended claim does not contain this spelling error, and therefore Applicants respectfully request withdrawal of this objection.

CLAIM REJECTIONS

A. The Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 7 and 8 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Specifically, the Examiner asserts that there is insufficient antecedent basis for the limitation "cell surface marker." In response, Applicants have amended claim 6 to recite this limitation, and thus the amended claim provides antecedent basis for claims 7 and 8. Therefore, Applicants respectfully request withdrawal of this rejection.

B. The Rejections Under 35 U.S.C. § 103

Claims 1, 4-9, 12, and 13 are rejected under 35 U.S.C. § 103 (a) as allegedly being obvious over McCabe *et al.* (*Toxicol. And Applied Pharmacol.*, 2001, vol. 177, pages 219-231) ("McCabe") in view of Nygaard *et al.* (Toxicol. 2002, vol. 174, pages 153-161) (Nygaard). Applicants respectfully disagree for the reasons set forth below.

Applicants note that Applicants have amended the independent claims and the amended claims are directed to "determining **beryllium sensitivity**...with...carboxy fluorescein diacetate succinimide ester (**CFSE**)." [emphasis added]. McCabe does not teach or suggest this claimed feature. Rather, McCabe relates to proliferation of alloantigen-reactive CD4-high T cells by exposing the cells to **lead**, not to beryllium. Lead and beryllium are completely different metals with different atomic numbers and functionalities. For example, lead's atomic number is 82, but beryllium's atomic number is 4. Lead can damage nervous connections and cause brain disorders. In contrast, beryllium compounds are category 1 carcinogens. Therefore, lead and beryllium are both

structurally and functionally different metals. Because of the diversity in genetic makeup and physiological responses to various metals and compounds, one cannot predict the beryllium sensitivity based on McCabe's lead exposed CD4 T cell proliferation. Therefore, the claimed invention is not obvious over McCabe.

Nygaard does not cure the defects in McCabe discussed above. Rather, Nyggard relates to blood and spleen lymphocyte parameters in rats treated with a single dose of immunosuppressant drug cyclophosphomide (CY). Therefore, McCabe and Nyggard, either alone or in combination, does not teach or suggest the claimed features discussed above.

Accordingly, the claimed invention is not obvious, and thus Applicants respectfully request withdrawal of the rejections.

Claims 1-13 are rejected under 35 U.S.C. § 103 (a) as allegedly being obvious over Fontenot *et al.* (*Journal of Clin. Invest.,* 2003, vol. 112 (5), pages 776-784 ("Fontenot"). Applicants respectfully disagree for the reasons set forth below.

The claimed invention is directed to "determining beryllium sensitivity…comprising staining a **peripheral blood leukocyte (PBL)**…with…CFSE." [emphasis added]. Fontenot does not teach or suggest this claimed feature. Rather, Fontenot relates to labeling branchoalveolar lavage (BAL) CD4 T cells with CFSE. The Examiner acknowledges that Fontenot does not teach "a method wherein PBL is used with CFSE in a beryllium sensitivity assay." However, the Examiner, without any factual data or support, merely asserts that one can substitute PBL T-cells for the Fontenot's BAL cells.

Applicants note that PBL cells and BAL cells are completely different cell types. For example, BAL cells contain components of the epithelial lining fluid (ELF) of lungs and often used to determine the protein composition of the pulmonary airways or pathogen levels in the lung. In contrast, peripheral blood leukocytes are composed of polymorphonuclear cells, including monocytes as well as lymphocytes. Elevated differential PBL cell counts, including counts of eosinophils, neutrophils, and monocytes

predict the future incidence of coronary arteary disease and diabetes. Therefore both BAL cells are different from PBL in terms of their source, type, and functionalities. Because of the diversity in genetic makeup and physiological mechanisms among various types of cells, they often respond differently to a metal, and therefore it is unpredictable to determine the beryllium sensitivity with PBL based on any alleged observation in BAL cells. Therefore, the claimed invention is not obvious over Fontenot.

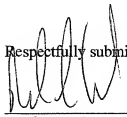
Applicants further note that Fontenot relates only to the antigen-specific CD4+ T cell response to beryllium. *See* Abstract of Fontenot. In contrast, Applicants' results clearly demonstrate CFSE-measured proliferative response for both CD4+ and CD8+ T Cells to beryllium. *See* Example 1 of the Specification. As described in the specification, "[f]inding a beryllium response in a population of...CD8+ T cells was unexpected." Therefore, for this additional reason, the claimed invention is unexpected and unpredictable in light of Fontenot. Accordingly, the claimed invention is not obvious, and thus Applicants respectfully request withdrawal of the rejections.

CONCLUSION

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 50-3355.



Respectfully submitted,

Mark S. Cohen
Attorney/Agent for Applicant(s)
Registration No. 42,425

Dated: September 9, 2009

Pearl Cohen Zedek Latzer, LLP
1500 Broadway, 12th Floor
New York, New York 10036
Tel: (646) 878-0800
Fax: (646) 878-0801